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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/679,231 | 10/03/2003 | Eric Charles Holland | D6534 | 3560 |

7590 06/20/2005

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EXAMINER

LIETO, LOUIS D

| ART UNIT | PAPER NUMBER |
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1632

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/679,231

Applicant(s)

HOLLAND, ERIC CHARLES

Examiner

Louis D. Lieto

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 18 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☐ Claim(s) _____ is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 3/21/2005 is acknowledged. Claims 1, 3 and 18 are pending in the instant application. Applicants canceled claims 2, 4-17 and 19-20, and amended claims 1, 3 and 18. The sections of title 35 U.S.C not included in this office action can be found in a previous office action. Applicant should note that the examiner of record is now Dr. Louis D. Lieto of ART UNIT 1632. An action on the merits follows.

Claim Objections

Claim 3 is newly objected to because of the following informalities: The status of Claim 3 is indicated as (original), however as is clear from the amendments to the claim text it should be identified as (currently amended). This new grounds of objection is necessitated by amendment. Appropriate correction is required.

Claim 18 is newly objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, the amendments to claim 3 cause it to be drawn to the same scope of the same subject matter as claim 18. This new grounds of objection is necessitated by amendment. Appropriate correction is required.

Claim Rejections - 35 USC § 112

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The rejection of original claims 1, 3 and 18 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. Applicant's arguments, amendments and cancellation of claims 2, 4-17 and 19-20 filed 3/21/2005 have been fully considered and were found persuasive in overcoming the remaining grounds of rejection.

The rejection of original claims 3 and 18 under 36 U.S.C. 112, first paragraph, for scope of enablement, is withdrawn. Applicant's arguments, amendments and cancellation of claims 2, 4-17 and 19-20 filed 3/21/2005 have been fully considered and were found persuasive in overcoming the remaining grounds of rejection.

The rejection of claim 1, drawn to a transgenic mouse, is maintained under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse expressing a reporter gene for a firefly luciferase protein, wherein said reporter gene is operably linked to an E2F1 promoter, does not reasonably provide enablement for a transgenic mouse expressing a gene encoding any luciferase protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 3/21/2005 have been fully considered but they are not persuasive. Claim 1 encompasses any luciferase protein, such as *Renilla mullerei* luciferase, *Pleuromamma* luciferase, *Gaussia princeps* luciferase, or Firefly luciferase. However, as noted in

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the previous action the specification only discloses making a transgenic mouse comprising Firefly luciferase.

In regards to the claimed embodiment comprising any protein capable of producing light upon metabolizing a substrate, the art teaches "'luciferase' is a family of photo-proteins that can be isolated from a large variety of insects, marine organisms, and prokaryotes. Luciferase proteins catalyzing the light-emitting reactions of firefly, coelenterates, or bacteria show no nucleotide homology to each other. The substrates 'luciferin of these reactions are also chemically unrelated.' Specific guidance to use a particular luciferase, therefore, does not necessarily predict guidance to use another luciferase. For example, Bhaumik and Gambhir (PNAS 99(1): 377-382, 2002) teach imaging of Rluc (Renilla luciferase) and Fluc (firefly luciferase) and show that the kinetics of light production are distinct wherein 'light from Rluc-carrying cells quickly peaks and rapidly extinguishes whereas light from Fluc-carrying cells peaks later and persists longer.' (pg. 382, paragraph 2). Further, the full embodiment of the claimed invention also encompasses reporter genes coding for non-luciferase proteins. Again, specific guidance to use a reporter gene that encodes firefly luciferase does not necessarily predict guidance to use a reporter gene that encodes any protein capable of producing light upon metabolizing a substrate because there are no known common structures or coding sequences that distinguish said proteins. Further, Vooijs et al., in discussing luciferase signal in bioluminescence imaging of spontaneous tumor formation, teaches 'in addition to signal location, signal strength is another parameter that determines sensitivity, which is determined by many factors including the number of luciferase-expressing cells, the promoter used to drive

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luciferase expression, the transgene copy number, and the transgene integration site." (pg. 1866, pgph 2).

Applicant argues that the emission spectra of most luciferases are sufficiently broad to extend to red wavelengths of greater than 600nm, thus allowing signal detection throughout the entire body of a mouse. While this may be true for Firefly luciferase, which has a λ_{\max} =575 nm {Steghens et al. (1998) Biochem J. 336:109-113; pg. 110, Fig. 1}, this is not true for luciferases such as the Metrida luciferase protein λ_{\max} =480 nm {Markova et al. (2004) J. Biol Chem. 279:3212-3217; pg. 3214, Fig. 1}. As can be seen in Fig. 1 of Markova et al. the strength of the bioluminescence emitted rapidly decrease as the wavelength reaches 600 nm. Applicant further argues since bioluminescent imaging via CCD camera provides for continuous real time imaging this overcomes any potential imaging problems due to differences between the emission spectra of luciferases. However, applicant does not provide any references or cite to where in the specification it is disclosed what minimum levels of photons>600 nm must be emitted by the relevant luciferase to overcome red light attenuation and be detected by an external CCD camera. Given the differences in λ_{\max} between Firefly luciferase and Metrida luciferase and the lack of specific guidance in the specification on the attenuation of photons>600 nm by a mouse body, the skilled practitioner would not be able to predict how to practice the claimed invention with Metrida luciferase or luciferases with similar λ_{\max} .

Further, applicant argues that any commercially available luciferase gene may be ligated to an E2F1 promoter to make a transgenic mouse. While the technology of making any vector is well known in the art, the difficulties of making any transgenic mouse are much more problematic. As stated in the previous office action of 3/21/2005 that factors influencing low

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expression, or lack thereof are not affected by copy number and such effects are seen in lines of transgenic mice made with the same construct. Further, see pages 4 and 5 of the previous action for a complete analysis on why the unpredictability of making transgenic animals, such as mice, is related to the site or sites of integration into the target genome. Because of the inherent unpredictability in the art of making transgenic animals, successful construction of a transgenic mouse expressing a firefly luciferase protein is not predictive of success for construction of mice expressing any other luciferase proteins. For the reasons of record stated above and in the action of 3/21/2005 the rejection over claim 1 is maintained.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3 and 18-19 under 35 U.S.C. 103(a) as being unpatentable over Hasan et al. (Genesis 29:1 16-122, 2001) in view of Muller et al (Mol Cell Biol 20(9): 3316-3329, 2000) is withdrawn. Applicant's arguments, amendments and cancellation of claims filed 3/21/2005 have been fully considered and were found persuasive in overcoming the remaining grounds of rejection.

No claims Allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-272-0735. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto


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